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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,817	02/26/2002	George F. Schreiner	SCIOS.002C1	8504

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EXAMINER	
SAOUD, CHRISTINE J	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 05/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,817	SCHREINER ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim 1 has been amended and claims 2-10 have been added in the amendment of 03 March 2004. Applicant should note that several issues were not addressed in the response. If the next response fails to address issues raised by the Examiner, it will not be considered a bona fide responsive amendment.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 03 March 2004 have been fully considered but they are not deemed to be persuasive.

Priority

The current status of all nonprovisional parent applications referenced should be included in the first line of the specification. Therefore, U.S. Pat. App. No. 09/392,932 should refer to U.S. Pat. No. 6,352,975. Correction is required. Applicant failed to address this issue in the response.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed (i.e. treatment of

hypertension, and not to compositions). Applicant failed to address this issue in the response.

The specification is objected to for an incomplete sentence at page 23, line 10. It is not clear what is intended by this partial sentence. Correction is required.

Claim Rejections - 35 USC § 112

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of salt-sensitive hypertension by the administration of VEGF, does not reasonably provide enablement for treatment of essential hypertension, as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The previous claim 1 was directed to the treatment of essential hypertension. The claim has been amended to recite "hypertension", however, the are recognizes two categories of hypertension; essential hypertension and hypertension with a known causality. The rejection is based on the fact that essential hypertension is encompassed by the instant claims.

The Declaration under 37 CFR 1.132 filed 03 March 2004 is insufficient to overcome the rejection of claim 1 based upon lack of enablement as set forth in the last Office action because: the animal model presented in the experiments would not be considered an appropriate model of hypertension by those of ordinary skill in the art to which the invention pertains, absent evidence to the contrary. The Declaration indicates

that a soluble VEGF receptor was expressed in rats using an engineered adenovirus, which resulted in hypertension. The hypertension was reversed by the administration of VEGF in these rats. However, this animal model of hypertension is not predictive of essential hypertension. This would be equivalent to creating hypertension by giving salt and then treating the hypertension by taking the salt away or giving a drug which elevates the blood pressure and then discontinuing the drug. Is the hypertension treated? Yes. Is this predictive of an individual with essential hypertension? No. Additionally, the model presented in the Declaration does not appear to be predictive of any known form of hypertension; it is a completely artificial form of hypertension that does not appear to correlate with any known form of hypertension in the general population, absent evidence to the contrary.

A review of the literature reveals that the accepted animal model for essential hypertension is the spontaneously hypertensive rat (SHR). See H'Doubler et al. (Laboratory Animal Science 41(5) : 471-473, 1991). The generally accepted control animal for the SHR rat is the Wistar Kyoto (WKY) rat because both strains were established from the same parenteral, normotensive Wistar stock.

Applicant asserts at page 6 of the response that "[e]ssential hypertension is associated with people who have an intake of salt exceeding 5.8 grams daily". Applicant has not provided a basis for this statement. Regardless, the data and evidence which has been presented is not persuasive because the animal models used are not art-accepted as predictive for essential hypertension for the reasons of record

and based on the teachings of the art which indicate that the accepted animal model for essential hypertension is the SHR rat,

At page 7 of the response, Applicant addresses the Declaration and the data contained therein. However, these arguments are not persuasive for the reasons give above. Namely, the experimentally derived mode of hypertension discussed in the Declaration is completely artificial and is not predictive of any known form of hypertension, absent evidence to the contrary. It is not unexpected that the administration of VEGF to these animals would reverse the condition of hypertension since the VEGF will bind the soluble VEGF receptor and thereby, eliminate it from animals. This effect does not reflect any biological activity that the VEGF may or may not have on the cardiovascular system to reduce blood pressure and therefore, is not predictive of a biological effect in an individual with essential hypertension.

Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 2 recites "wherein filtration or excretion of a solute is improved as compared to the pre-treatment condition of the patient". However, "solute" is not defined and would encompass any agent that could be dissolved in any liquid since the claim fails to indicate what organ or process is doing the filtration or excretion. A reading of the specification would indicate that salts may be intended, but claim 2 does

not limit the "solute" to salts. Secondly, there is no evidence of record which would support the position that the filtration or excretion of solutes is improved by the administration of VEGF to an individual (see example 4 of the specification).

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on mttr, 8:00-2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud